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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,671	09/24/2001	Antonio Parente Duena	P/ 189-162	4516

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,671	DUENA ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment of Papers Received: Amendment/Response filed 12/15/03.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by BIOGRAM AM (WO 97/14408). The claims are drawn to a pharmaceutical preparation comprising lactic-co-glycolic copolymer, which incorporates a peptide, and a citric acid ester.

BIOGRAM AM discloses a microcapsule comprising PLGA (poly lactic/glycolic acid) comprising proteins, and peptides and triethyl citrate as an additive (pg.8, lin. 1-14; pg. 10, lin. 29 – pg. 11, lin. 10, claims). These disclosures along with others render the claims anticipated.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over BIOGRAM AB (WO 97/14408). The claims are drawn to a microcapsule formulation comprising a peptide, lactic-co-glycolic acid and a citric acid ester. The claims recite concentrations of the citric acid ester and proportions for the lactic acid and glycolic acid in the copolymer.

BIOGRAM discloses general formulation comprising PLGA and triethyl citrate as an additive. The reference is lacking specific teachings to the concentrations of the citric acid esters and the proportions of the copolymer acids. However it has been held that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various pharmaceutical compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

With this in mind it would have been obvious to one of ordinary skill in the art to maximize the concentrations and proportions of the formulations of BIOGRAM in order to deliver the optimum formulation and improve the delivery of the bioactive agent. It would have

been obvious to a skilled artisan to follow the suggestions of the art and maximize and optimize the concentrations of citric acid ester and copolymer with an expected result of a pharmaceutical formulation useful in delivering peptides and proteins to treat disorders.

6. Claims 6 – 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over BIOGRAM AB (WO 97/14408) in view of Yamamoto et al (USPN 4,954,298), Bodmer et al (USPN 5,538,739) and Canal et al (USPN 5,536,508). The claims are drawn to a pharmaceutical dosage form comprising lactic-co-glycolic copolymer, a citric acid ester and various species of peptides.

As discussed above BIOGRAM discloses a microcapsule formulation comprising lactic-co-glycolic acid copolymer, triethyl citrate, and various peptides and proteins. The reference however does not disclose the specific species of peptides, though the reference suggests the inclusion of peptides into the formulation. It would be well within the level of skill in the art to include these species into the formulation of BIOGRAM.

Yamamoto et al teaches essential elements of claims 5-7. The reference teaches a microcapsule sustained-release formulation comprising a biodegradable copolymer of lactic/glycolic acid, and a LHRH derivative, leuprolide (Abstract; column 2, lines 28-32; Examples 2, 4 and 5). The reference also teaches the concentrations of the claimed invention for the lactic/glycolic copolymer (column 5, lines 26-36).

Bodmer et al teaches essential elements of claims 5, 8 and 9. The reference teaches a microcapsule sustained-release formulation comprising a biodegradable copolymer of lactic/glycolic acid, and a somatostatine analogue, octreotide (Abstract; column 4, lines 18-25; Examples; claims1-5).

Canal et al teaches essential elements of claims 5, 10 and 11. The reference teaches a microcapsule sustained-release formulation comprising a biodegradable copolymer of lactic/glycolic acid, and a calcitonine analogue, salmon calcitonine (Abstract; column 4, lines 30-36; Examples 15 and T).

These references disclose specific peptides in combination with lactic/glycolic acid copolymers and would be suitable to be included in the formulations of BIOGRAM. One of ordinary skill in the art would have been motivated to include these compounds under the suggestion of BIOGRAM and the individual references. BIOGRAM discloses the inclusion of peptides, while the references disclose the peptides in lactic/glycolic copolymer formulations. A skilled artisan would have been motivated to make the substitutions in order to impart particular prophylactic properties onto the formulation of BIOGRAM. It would have been obvious to combine the references with an expected result of a microcapsule formulation useful for the treatment of various disorders.

Response to Arguments

7. Applicant's arguments filed 12/15/03 have been fully considered but they are not persuasive. Applicant argues that:

a. The prior art does not disclose that the peptide is not on the surface and therefore does not anticipate nor obviate the instant invention.

With regard to this argument, it is the position of the examiner that applicant has yet to distinctly point out the importance of the placement of the active agent within the structure of the formulation. The prior art presents a microcapsule formulation comprising a peptide, and a polymer. Barring a showing of criticality to the placement of the peptide, whether on the surface

of the microcapsule, in the center or evenly distributed throughout the claims will remain obviated by the prior art. A showing of unexpected results to the placement of the active agent is required, since the cited art of BIOGRAM presents formulations within the same field of endeavor, and accomplish the same results of treating various disorders. Applicant is reminded that the Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. *See Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). For these reasons the claims will remain anticipated an obviated by the prior art.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 571-272-0608. The examiner can normally be reached on M-F 7:00-4:30 every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Micah-Paul Young
Examiner
Art Unit 1615

MP Young

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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